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LIPOPROTEIN(A) IN FAMILIAL HYPERCHOLESTEROLEMIA WITH PROPROTEIN CONVERTASE SUBTILISIN KEXIN TYPE 9 GAIN-OF-FUNCTION MUTATIONS: IMPLICATION OF RESIDUAL RISK IN STATIN-ERA

Poster Contributions
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Background: Lipoprotein(a) [Lp(a)] is an established residual risk factor for cardiovascular disease. PCSK9 inhibitors have been reported to reduce Lp(a) up to ~30%, the mechanism of which remains unclear. In addition, few data exist regarding the Lp(a) levels in patients with gain-of-function proprotein convertase subtilisin kexin type 9 (PCSK9) mutations.

Background: We aimed to determine whether the patients with familial hypercholesterolemia (FH) due to the gain-of-function mutations in PCSK9 gene exhibit higher Lp(a) level as well as higher incidents of cardiovascular disease compared to those in patients with LDLR mutation or to those in normal controls.

Methods and Results: Nineteen mutation-determined heterozygous FH patients with gain-of-function PCSK9 mutation (FH-PCSK9, mean age=38yr, male=9, mean LDL cholesterol=264±58mg/dl), 68 mutation-determined heterozygous FH patients with LDLR mutations (FH-LDLR, mean age=40yr, male=37, mean LDL cholesterol=245mg/dl), and 34 controls (CONTROLS, mean age=62yr, male=20, mean LDL cholesterol=108mg/dl) were evaluated. We assessed their total cholesterol, triglyceride, HDL cholesterol, LDL cholesterol, the presence of coronary artery disease, and Lp(a) levels. There were no significant differences of LP(a) levels of among those 3 groups (FH-PCSK9, FH-LDLR, and CONTROLS, median Lp(a)=20.7mg/dl [IQR:11.0-37.6], 23,4 mg/dl [IQR:15.1-40.0], 21.0mg/dl [IQR:13.2-31.3], respectively, Mann-Whitney U test). Also there was no difference between the presence of coronary artery disease in FH-PCSK9 and that of FH-LDLR (15.8% vs. 17.6%, Chi-square test).

Conclusion: These data suggest that the mechanism of reduction in Lp(a) through PCSK9 inhibitor might be related with independent pathway(s) of LDL and LDLR. Such unknown pathway(s) could be new therapeutic target(s) for the residual risk in this statin-era.